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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/621,958	07/16/2003	Steven J. Locke	357000-1200	2039

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FOLEY & LARDNER LLP
1530 PAGE MILL ROAD
PALO ALTO, CA 94304

EXAMINER

VENCI, DAVID J

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 09/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/621,958	LOCKE & PINTO	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on June 8, 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 4-23, 28 and 32-36 is/are pending in the application.
- 4a) Of the above claim(s) 28 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 4-23 and 32-36 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 4-23, 28 and 32-36 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>06/08/06</u> . | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Examiner acknowledges Applicants' reply, filed June 8, 2006, which cancelled claims 1-3, 24-27 and 29-31, and added new claims 32-36.

Currently, claims 4-23 and 32-36 are under examination. Claim 28 is drawn to a non-elected invention and remains withdrawn from consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112 – second paragraph

Claims 4-23 and 32-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Throughout the claims, the phrase "differential isotope labeled reagents" is indefinite. The number of chemically distinct reagents is not clear. The number of isotopically distinct reagents is not clear.

Claim Rejections - 35 USC § 102

Claims 4-15, 17-23 and 32-36 are rejected under 35 U.S.C. 102(e) as being anticipated by Aebersold *et al.* (US 6,670,194). With respect to independent claim 36:

Aebersold *et al.* describe a method for analysis of at least three samples (see col. 13, line 47, "more than two samples") of cellular extracts (see col. 5, line 63, "cell or tissue lysates") comprising molecules, wherein the molecules have an amine bearing an active hydrogen (see col. 10, lines 30-41, "PRGs... include... those that react with amino groups"), the method comprising:

(i) providing at least three combinations of differential isotope labeled reagents (see col. 13, lines 47-49, "sets of identical tagged peptides in which each set member is differentially isotopically labeled"), wherein each of the at least three combinations of differential isotope labeled reagents comprises at least two chemically distinct reagents (see *e.g.*, col. 10, line 30, "protein reactive group"; see *also* lines 51-52, "aldehydes or ketones in the presence... of NaBH₄ or NaCNBH₃") (paraphrasing mine), and the at least two chemically distinct reagents are present in each of the at least three combinations of differential isotope labeled reagents (see col. 13, lines 47-49, "sets of identical tagged peptides") (emphasis added), and each of the at least three combinations of differential isotope reagents is isotopically distinct (see col. 13, lines 47-49, "differentially isotopically labeled");

(ii) reacting (a) a first sample with (b) a first combination of differential isotope labeled reagents, reacting (c) a second sample with (d) a second combination of differential isotope labeled reagents, and reacting (e) a third sample with (f) a third combination of differential isotope labeled reagents (see col. 11, lines 37-38, "the proteins in each sample are reacted with affinity tagging reagents"), wherein the reacting results in a reductive alkylation of the amine of the molecule to alkylamine derivatives (see col. 10, lines 50-52, "aldehydes or ketones in the presence... of

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NaBH₄ or NaCNBH₃) (paraphrasing mine), such that the derivatives are labeled at an alkylamine (see col. 8, lines 27-30, "any one or more of the hydrogen, nitrogen, oxygen or sulfur atoms in the linker may be replaced with their isotopically stable isotope");

(iii) combining the derivatives (see col. 6, lines 2-3, "The treated samples are then combined");

(iv) separating the derivatized molecules into fractions (see col. 36, lines 11-12, "separated by 1D or 2D gel electrophoresis");

(v) enzymatically cleaving the derivatized molecules (see col. 19, lines 41-43, "proteolysis");

(vi) separating the fragments (see col. 19, lines 41-43, "isolated by affinity chromatography");

(vii) examining the derivatives by mass spectrometry (see Abstract, "reaction products are characterized by mass spectrometric (MS) techniques"); and

(viii) sequencing the fragments (see col. 36, lines 19-36, "CID spectrum of a peptide contains sufficient information to identify the protein by searching sequence databases").

Claim Rejections - 35 USC § 103

Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over Aebersold *et al.* (US 6,670,194) in view of Vandekerckhove & Gevaert (US 2004/0005633).

Aebersold *et al.* teach a method for the simultaneous quantitative analysis of at least three samples as substantially described, *supra*, and incorporated herein.

Aebersold *et al.* do not teach a method wherein formaldehyde and acetaldehyde are used.

However, Vandekerckhove & Gevaert teach the use of deuterated formaldehyde and acetaldehyde (see para. [0107]) in order to induce a distinguishable mass shift in peptide analysis.

It would have been obvious for a person of ordinary skill in the art to modify the method of Aebersold *et al.* with the use of formaldehyde and acetaldehyde because Vandekerckhove & Gevaert teach that such reactions are "known to proceed in mild conditions" and "may lead to the incorporation of a predictable number of deuterium atoms" (see para. [0107]).

Response to Arguments

In prior Office Action, claims 1-27 and 29 were rejected under 35 U.S.C. 102(e) or 35 U.S.C. 103(a) in view of various combinations of teachings of Aebersold *et al.* (US 6,670,194), Figeys *et al.* (US 2002/0076817) and Vandekerckhove & Gevaert (US 2004/0005633).

In response, Applicants set forth three arguments enumerated in Applicants' reply, pp. 13-17.

Applicants' arguments have been carefully considered but are not persuasive.

Applicants' arguments that Aebersold *et al.* fail to show certain features of Applicants' invention (e.g., specific aldehydes, reducing agents, solvents, etc.) is not persuasive because these features are not recited in the rejected claims. Applicants' invention, *as claimed*, does not recite a specific derivatization agent. Although claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Examiner acknowledges that Aebersold *et al.* describe analytical reagents that include linkers ("L"), protein reactive groups ("PRG") and affinity labels ("A"). However, the mere fact that Aebersold *et al.* characterize their reagent using alphanumeric symbols A—L—PRG does not detract from the reality that Aebersold *et al.* describe differentially labeled isotope reagents. Insofar as Applicants' invention, *as claimed*, merely requires "differential isotope labeled reagents", Examiner posits that Aebersold's description of "analytical reagents" is sufficient to anticipate Applicants' invention, *as claimed*.

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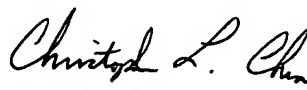
Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Examiner
Art Unit 1641

djv


CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641
2/21/06